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## **Claims**

- 1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of at least one of
- 5 SEQ ID NO.: 2, SEQ ID NO.: 4 and SEQ ID NO.: 6

for use as a medicament.

- 2. An isolated polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO.: 2, SEQ IN NO.: 4 and SEQ ID NO.: 6.
  - 3. An isolated polypeptide according to claim 1 or 2, wherein said amino acid sequence is a sub-sequence of with a minimum length of 10 amino acids.
- 15 4. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:2.
  - 5. A polypeptide according to claim 4, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:2.

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- 6. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:4.
- 7. A polypeptide according to claim 6, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:4.
  - 8. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:6.
- 30 9. A polypeptide according to claim 8, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:6.
  - 10. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:2.

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11. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:4.

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- 12. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:6.
- 13. An polypeptide to claim 1-12, wherein said amino acid is consistently up-regulated
  after antibody selection-induced change from VSA<sub>UM</sub> to VSA<sub>SM</sub> expression.
  - 14. An polypeptide according to claim 1-13, wherein said amino acid sequence is capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not to the CD36 receptor.
- 15. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of at least one of
  - a) SEQ ID NO.: 1, SEQ ID NO.: 3 SEQ ID NO.: 5 and SEQ ID NO.; 7,

for use as a medicament.

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- 16. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO.: 1, SEQ ID NO.: 3 SEQ ID NO.: 5 or SEQ ID NO.; 7.
- 17. A nucleic acid according to claim 15-16, wherein said nucleotide sequence is a subsequence of with a minimum length of 30 nucleotides.
- 25 18. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:1.
  - 19. A nucleic acid according to claim 18, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:1.
  - 20. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:3.
- 21. A nucleic acid according to claim 20, wherein said nucleic acid consists of thenucleotide sequence shown in SEQ ID NO:3.
  - 22. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:5.

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23. A nucleic acid according to claim 22, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:5.

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- 24. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotidesequence shown in SEQ ID NO:7.
  - 25. A nucleic acid according to claim 24, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:7.
- 10 26. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:1.
  - 27. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:3.
  - 28. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:5.
- 29. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least80% sequence identity to SEQ ID NO:7.
  - 30. A nucleic acid sequence according to claim 15-29, wherein said sequence is consistently upregulated after antibody selection-induced change from  $VSA_{SM}$  expression.
  - 31. A nucleic acid according to claim 15-30, wherein said nucleic acid sequence encodes a polypeptide which is capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not the CD36 receptor.
- 30 32. A recombinant vector comprising the nucleic acid defined in any of claims 15-31 operably linked to one or more control sequences for use as a medicament
- 33. A composition comprising a polypeptide according to any of claims 1-14 or a nucleic acid according to any of claims 15-31 and a pharmaceutically acceptable diluent, carrier or35 adjuvant.
  - 34. A composition according to claim 33, wherein said composition is an immunogenic composition.

- 35. A composition according to claim 34, wherein said composition induces an IgG/IgM antibody response.
- 36. An isolated antibody or isolated antiserum induced in response to one or more polypeptides as defined in any of claims 1-14 and/or to one or more nucleic acids as defined in any of claims 15-31.
- 37. An antibody according to claim 36, wherein said antibody is capable of binding to a molecule expressed on the surface of an intact erythrocyte infected by a parasite causing malaria.
  - 38. An antibody according to claim 36, wherein said antibody is capable of recognising parasites selected *in vitro* for expression of VSA<sub>SM</sub>.
- 39. An antibody according to claim 36, wherein said antibody is capable of binding to a molecule expressed on the surface of an intact erythrocyte infected by a parasite capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not the CD36 receptor.
- 20 40. A vaccine comprising at least one nucleic acid according to any of claims 15-31 or at least one vector according to claim 32, the vaccine effecting *in vivo* expression of at least one antigen by a subject, to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to malaria caused by *Plasmodium falciparum*.

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- 41. Use of a polypeptide according to any of claims 1-14 for the manufacture of a composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.
- 30 42. Use of a polypeptide according to any of claims 1-14 for the manufacture of a vaccine for malaria prophylaxis.
  - 43. Use of a polypeptide according to any of claims 1-12 for the manufacture of a composition for vaccination against malaria.

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44. Use of a nucleic acid according to any of claims 15-31 for the manufacture of an composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.

- 45. Use of a nucleic acid according to any of claims 1-31 for the manufacture of a vaccine for malaria prophylaxis.
- 46. Use of a nucleic acid according to any of claims 15-31 for the manufacture of a composition for vaccination against malaria.
  - 47. Use of a recombinant vector according to claim 32 for the manufacture of a composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.
  - 48. Use of a recombinant vector according to claim 32 for the manufacture of a vaccine for prophylactic treatment of severe malaria.
- 49. Use of a recombinant vector according to claim 32 for the manufacture of a composition for vaccination against severe malaria.

- 50. Use according to any of claims 41-49, wherein said malaria is caused by *Plasmodium falciparum*.
- 20 51. A method for prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in an subject said method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-31 or a recombinant vector according to claim 32.
- 25 52. A method for the prophylactic treatment of severe malaria in an subject, said method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-31 or a recombinant vector according to claim 32.
- 30 53. A vaccination method against severe malaria in an subject, said vaccination method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-31 or a recombinant vector according to claim 32.
- 35 54. A vaccine comprising any of the polypeptides according to any of claims 1-14, the nucleic acids according to any of claims 15-31 or the recombinant vector according to claim 32, said vaccine characterised in that it induces an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by a parasites.

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- 56. A DNA vaccine, which results in the expression of a polypeptide comprising one or more B-cell and/or T cell epitopes from any of the polypeptide sequences according to claim 1-14, wherein said vaccine is capable of inducing an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by parasites.
- 15 57. A DNA vaccine comprising at least one nucleic acid sequences according 15-31, wherein said vaccine is capable of inducing an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by parasites.
- 20 58. An *in vitro* diagnostic method, said method comprising contacting a sample with a polypeptide according to any of claims 1-14 under conditions allowing an *in vitro* immunological reaction to occur between said polypeptide and the antibodies possibly present in said sample, and *in vitro* detect the antigen-antibody complexes possibly formed.

59. An *in vitro* diagnostic method according to claim 58, wherein a disease-state profile for a tested subject is generated by determining the concentration or expression level in a sample of sequences as defined in any of claims 1-14 and/or 15-31.

30 60. An in vitro diagnostic kit comprising

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parasites.

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- a) a sequence as defined in any of claims 1-14 and/or 15-31
- b) reagents for preparing a suitable medium for carrying out an immunological reaction between an antibody present in a sample of body fluid or tissue and said sequence; and
- c) reagents allowing the detection of the antigen-antibody complexes formed, wherein said reagents may bear a radioactive or non-radioactive label.
- 61. A method for generating a vaccine against severe malaria comprising

- a) injecting a sequence according to any of claims 1-14 in a subject
- b) enabling said subject to generate antibodies specifically recognising any of the polypeptide sequences according to claim 1-14
- c) purify said antibodies
- d) selecting antibodies having cross-reactivity to parasites causing severe malaria
  - e) selecting antibodies having the ability to inhibit adhesion to endothelial cells.
  - 62. A method for testing an inhibitor-molecule capable of inhibiting binding of any of the polypeptides according to claim 1-14 to a receptor expressed on endothelia cells
- 10 comprising
- a) in vitro cultures of endothelial cells
- b) add potential inhibiting-molecule
- c) add RBC infected with parasites, said iRBC expressing any of said polypeptide sequences on their surface of the RBC
- d) measure the binding of the iRCB with said endothelia cells by microscopy or other means of quantifying binding as for instance liquid scintillation spectrometry.